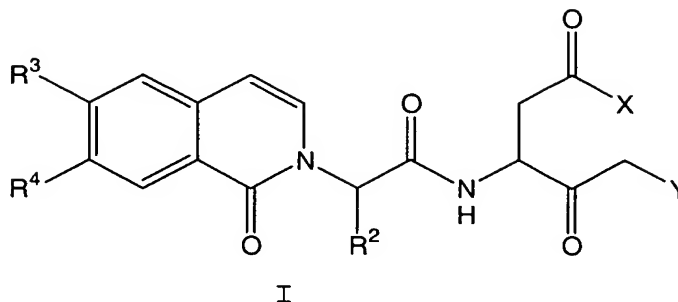


We claim:

1. A compound of formula I:



5 wherein:

X is $-OR^1$ or $-N(R^5)_2$,

Y is halo, trifluorophenoxy, or tetrafluorophenoxy;

R^1 is:

10 C_{1-6} straight chained or branched alkyl, alkenyl, or alkynyl, wherein the alkyl, alkenyl, or alkynyl is optionally substituted with aryl, CF_3 , Cl, F, OMe, OEt, OCF_3 , CN, or NMe_2 ;

C_{1-6} cycloalkyl, wherein 1-2 carbon atoms in the cycloalkyl is optionally replaced with $-O-$ or $-NR^5-$;

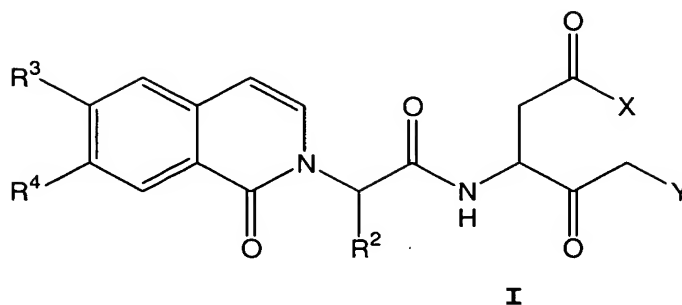
15 R^2 is C_{1-6} straight chained or branched alkyl;

R^3 is hydrogen, halo, OCF_3 , CN, or CF_3 ;

R^4 is hydrogen, halo, OCF_3 , CN, or CF_3 ; and

20 each R^5 is independently H, C_{1-6} straight chained or branched alkyl, aryl, $-O-C_{1-6}$ straight chained or branched alkyl, or $-O$ -aryl.

2. A compound of formula I:



wherein:

- 5 X is $-OR^1$ or $-N(R^5)_2$,
 Y is halo, trifluorophenoxy, or tetrafluorophenoxy;
 R^1 is:

C_{1-6} straight chained or branched alkyl,
 alkenyl, or alkynyl, wherein the alkyl, alkenyl, or
 10 alkynyl is optionally substituted with optionally
 substituted aryl, CF_3 , Cl, F, OMe, OEt, OCF_3 , CN, or NMe_2 ;

C_{1-6} cycloalkyl, wherein 1-2 carbon atoms in the
 cycloalkyl is optionally replaced with $-O-$ or $-NR^5-$;

- R^2 is C_{1-6} straight chained or branched alkyl;
 15 R^3 is hydrogen, halo, OCF_3 , CN, or CF_3 ;
 R^4 is hydrogen, halo, OCF_3 , CN, or CF_3 ; and
 R^5 is H, C_{1-6} straight chained or branched alkyl, or
 $-O-C_{1-6}$ straight chained or branched alkyl; provided that
 if:

- 20 Y is F;
 R^2 is isopropyl, R^3 is hydrogen, and R^4 is Cl; or
 R^2 is ethyl, R^3 is hydrogen, and R^4 is Cl or CF_3 ; or
 R^2 is ethyl, R^3 is Cl or CF_3 , and R^4 is hydrogen; then
 R^1 is not t-butyl; and if

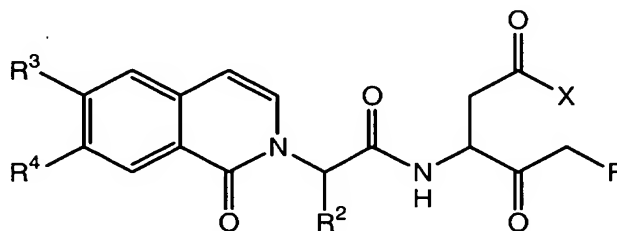
- 25 Y is 2,3,5,6-tetrafluorophenoxy;
 R^2 is ethyl; and
 R^3 and R^4 are each hydrogen; or

R^3 is hydrogen and R^4 is Cl or CF_3 ; or
 R^3 and R^4 are each Cl; then
 R^1 is not t-butyl.

5 3. The compound according to claim 1 or
claim 2, wherein R^2 is ethyl, n-propyl, or isopropyl.

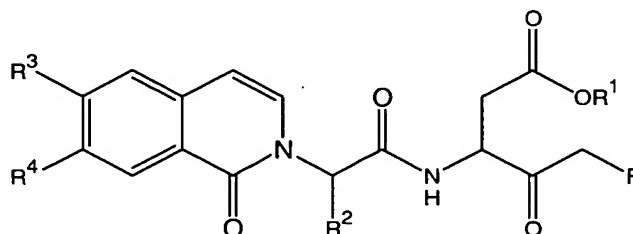
 4. The compound according to any one of claims
1-3, wherein Y is F, trifluorophenoxy, or
10 tetrafluorophenoxy.

 5. The compound according to claims 1 or 2,
having formula IA':



15 R^2 is ethyl, n-propyl, or isopropyl;
 R^3 is hydrogen, halo, OCF_3 , CN, or CF_3 ; and
 R^4 is hydrogen, halo, OCF_3 , CN, or CF_3 .

20 6. The compound according to claims 1 or 2,
having formula IA:

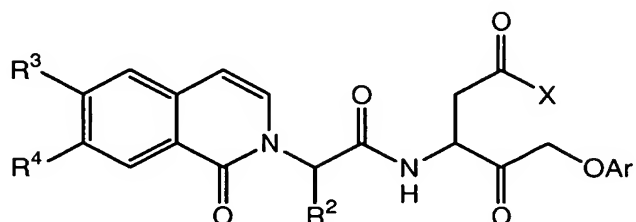


R^1 is C_{1-6} straight chained or branched alkyl
optionally substituted with phenyl or CF_3 ;
25 R^2 is ethyl, n-propyl, or isopropyl;

R^3 is hydrogen, halo, OCF_3 , CN, or CF_3 ; and

R^4 is hydrogen, halo, OCF_3 , CN, or CF_3 .

7. The compound according to claims 1 or 2,
5 having the formula IB':



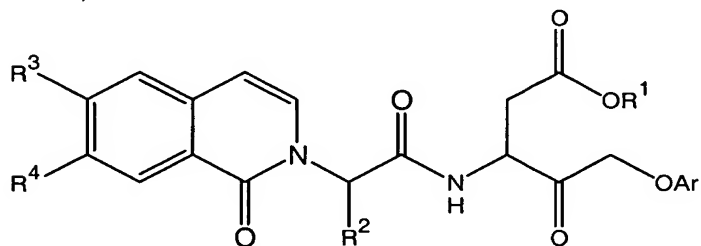
wherein:

R^2 is ethyl, n-propyl, or isopropyl;

10 R^3 and R^4 are each independently hydrogen, halo,
 OCF_3 , CN, or CF_3 ; and

Ar is trifluorophenyl or tetrafluorophenyl.

8. The compound according to claims 1 or 2,
15 having the formula IB:



wherein:

R^1 is C_{1-6} straight chained or branched alkyl
optionally substituted with phenyl or CF_3 ;

20 R^2 is ethyl, n-propyl, or isopropyl;

R^3 and R^4 are each independently hydrogen, halo,
 OCF_3 , CN, or CF_3 ; and

Ar is trifluorophenyl or tetrafluorophenyl.

9. The compound according to claim 8, wherein Ar is 2,3,5,6-tetrafluorophenyl.

10. The compound according to any one of claims 1-9, wherein R^2 is ethyl.

11. The compound according to any one of claims 1-10, wherein R^3 is H, and R^4 is F, Cl, or CF_3 .

12. The compound according to any one of claims 1-6 and 10-11 wherein when Y is halo, then R^3 and R^4 , are not simultaneously hydrogen.

13. The compound according to any one of claims 1-12 wherein X is $-OR^1$ and the R^1 is an alkyl group that is not substituted with phenyl or CF_3 .

14. The compound according to any one of claims 1-13 wherein X is $-OR^1$ and the R^1 is ethyl or propyl.

15. The compound according to any one of claims 1-5, 7, or 10-12 wherein X is $-N(R^5)_2$.

16. The compound according to claim 15 wherein X is $-N(R^5)_2$ and one R^5 is C_{1-6} straight chained or branched alkyl and the other R^5 is $-O-C_{1-6}$ straight chained or branched alkyl.

17. The compound according to claim 15 wherein X is $-N(R^5)_2$ and one R^5 is H or $-C_{1-6}$ straight chained or

branched alkyl and the other R⁵ is -C₁₋₆ straight chained or branched alkyl.

18. The compound according to any one of
5 claims 15-17 wherein R⁵ is methyl, ethyl, or propyl.

19. A compound selected from Table 1.

20. A pharmaceutical composition comprising:
10 a) a compound according to any one of claims 1-19; and
b) a pharmaceutically acceptable carrier, adjuvant or vehicle.

15 21. The composition according to claim 20, wherein said compound is selected from a compound according to any one of claims 1, 2, 5, 6, 7, 8, or 18.

22. A method for treating a disease in a
20 patient, wherein said disease is an IL-1 mediated disease, an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a destructive bone disorder, a proliferative disorder, an infectious disease, a degenerative disease, a disease associated
25 with cell death, an excess dietary alcohol intake disease, a viral mediated disease, retinal disorders, uveitis, inflammatory peritonitis, osteoarthritis, pancreatitis, asthma, adult respiratory distress syndrome, glomerulonephritis, rheumatoid arthritis,
30 systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune

neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, inflammatory bowel disease, Crohn's disease, psoriasis, atopic dermatitis, scarring, graft vs host disease, organ transplant rejection, organ apoptosis
5 after burn injury, osteoporosis, leukemias and related disorders, myelodysplastic syndrome, multiple myeloma-related bone disorder, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, hemorrhagic shock,
10 sepsis, septic shock, burns, Shigellosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Kennedy's disease, prion disease, cerebral ischemia, epilepsy, myocardial ischemia, acute and chronic heart disease, myocardial infarction, congestive heart failure,
15 atherosclerosis, coronary artery bypass graft, spinal muscular atrophy, amyotrophic lateral sclerosis, multiple sclerosis, HIV-related encephalitis, aging, alopecia, neurological damage due to stroke, ulcerative colitis, traumatic brain injury, spinal cord injury, hepatitis-B,
20 hepatitis-C, hepatitis-G, yellow fever, dengue fever, Japanese encephalitis, various forms of liver disease, renal disease, polycystic kidney disease, H. pylori-associated gastric and duodenal ulcer disease, HIV infection, tuberculosis, or meningitis;
25 said method comprising the step of administering to said patient compound according to any one of claims 1-19 or a pharmaceutical composition according to any one of claims 20-21.

30 23. The method according to claim 22, wherein the disease is an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a

destructive bone disorder, a proliferative disorder, an infectious disease, a degenerative disease, a disease associated with cell death, an excess dietary alcohol intake disease, a viral mediated disease, inflammatory
5 peritonitis, glomerulonephritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, scarring, graft vs host disease, organ transplant rejection, organ apoptosis after burn injury, osteoporosis, leukemias and
10 related disorders, myelodysplastic syndrome, metastatic melanoma, hemorrhagic shock, sepsis, septic shock, burns, Shigellosis, Alzheimer's disease, Parkinson's disease, Huntington's disease, Kennedy's disease, prion disease, cerebral ischemia, epilepsy, myocardial ischemia, acute
15 and chronic heart disease, myocardial infarction, congestive heart failure, atherosclerosis, coronary artery bypass graft, spinal muscular atrophy, amyotrophic lateral sclerosis, multiple sclerosis, HIV-related encephalitis, aging, alopecia, neurological damage due to
20 stroke, traumatic brain injury, spinal chord injury, hepatitis-B, hepatitis-C, hepatitis-G, various forms of liver disease, renal disease, polycystic kidney disease, H. pylori-associated gastric and duodenal ulcer disease, HIV infection, tuberculosis, and meningitis.

25

24. The method according to claim 22, wherein the disease is neurological damage due to stroke, traumatic brain injury, spinal cord injury, Alzheimer's disease, Parkinson's disease, Huntington's disease,
30 multiple sclerosis, or cerebral ischemia.

25. The method according to claim 22, wherein the disease is osteoarthritis, pancreatitis, asthma, adult respiratory distress syndrome, glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Grave's disease, autoimmune gastritis, insulin-dependent diabetes mellitus (Type I), autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, chronic active hepatitis, myasthenia gravis, inflammatory bowel disease, Crohn's disease, psoriasis, graft vs host disease, osteoporosis, multiple myeloma-related bone disorder, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, sepsis, septic shock, Shigellosis, cerebral ischemia, myocardial ischemia, spinal muscular atrophy, or neurological damage due to stroke.

26. The method according to claim 22, wherein the disease is an IL-1 mediated disease, an apoptosis mediated disease, an inflammatory disease, an autoimmune disease, a destructive bone disorder, a proliferative disorder, an infectious disease, a degenerative disease, a disease associated with cell death, an excess dietary alcohol intake disease, inflammatory peritonitis, osteoarthritis, pancreatitis, adult respiratory distress syndrome, rheumatoid arthritis, chronic active hepatitis, inflammatory bowel disease, Crohn's disease, psoriasis, atopic dermatitis, organ apoptosis after burn injury, hemorrhagic shock, sepsis, septic shock, burns, Alzheimer's disease, Parkinson's disease, Huntington's disease, cerebral ischemia, myocardial ischemia, acute and chronic heart disease, myocardial infarction, congestive heart failure, coronary artery bypass graft,

amyotrophic lateral sclerosis, multiple sclerosis,
alopecia, neurological damage due to stroke, ulcerative
colitis, traumatic brain injury, spinal cord injury,
hepatitis-B, hepatitis-C, hepatitis-G, various forms of
5 liver disease, or renal disease.

27. The method according to claim 22, wherein
said disease is a complication associated with a coronary
artery bypass graft.

10

28. A method for inhibiting a caspase-mediated
function in a patient comprising the step of
administering to said patient a compound according to any
one of claims 1-19 or a pharmaceutical composition
15 according to any one of claims 20-21.

29. The method according to claim 28, wherein
the function occurs in the central nervous system.

20 30. The method according to claim 28, for
decreasing IGIF or IFN- γ production in a patient.

31. The method according to claim 30, wherein
the IGIF or IFN- γ production is in the central nervous
25 system.

32. The method according to any one of claims
22-31 wherein said composition comprises an additional
therapeutic agent.

30

33. A method of preserving cells, said method
comprising the step of bathing the cells in a solution of

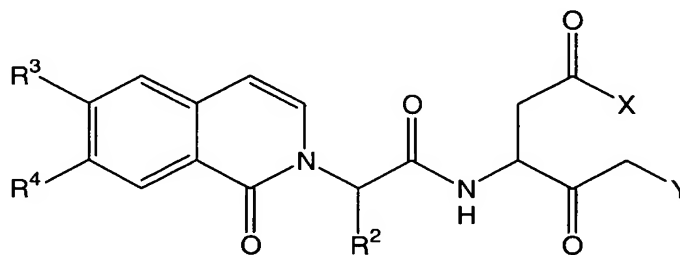
the compound according to any one of claims 1-19 or a pharmaceutically acceptable derivative thereof.

34. The method according to claim 33, wherein
5 said cells are in:

- a) an organ intended for transplant; or
- b) a blood product.

35. A method of treating cancer using
10 immunotherapy, wherein said immunotherapy comprises as a component thereof a compound according to any one of claims 1-19.

36. A process for preparing a compound of
15 formula I:



wherein:

20 X is $-OR^1$ or $-N(R^5)_2$,
Y is halo, trifluorophenoxy, or tetrafluorophenoxy;
R¹ is:

C₁₋₆ straight chained or branched alkyl,
alkenyl, or alkynyl, wherein the alkyl, alkenyl, or
25 alkynyl is optionally substituted with optionally
substituted phenyl, CF₃, Cl, F, OMe, OEt, OCF₃, CN, or
NMe₂;

C₁₋₆ cycloalkyl, wherein 1-2 carbon atoms in the cycloalkyl is optionally replaced with -O- or -NR⁵-;

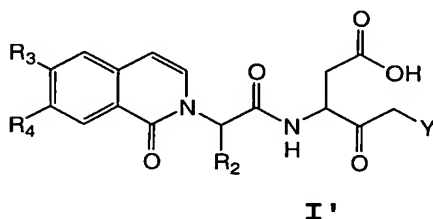
R² is C₁₋₆ straight chained or branched alkyl;

R³ is hydrogen, halo, OCF₃, CN, or CF₃;

5 R⁴ is hydrogen, halo, OCF₃, CN, or CF₃; and

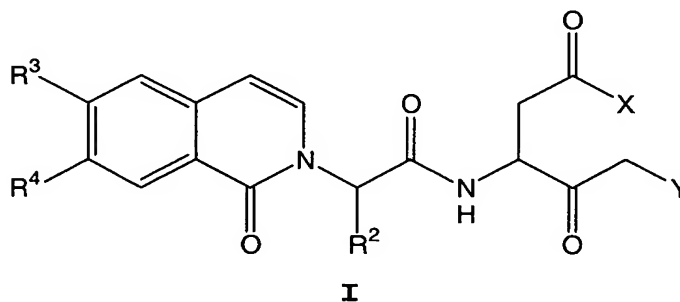
R⁵ is H, C₁₋₆ straight chained or branched alkyl, aryl, -O-C₁₋₆ straight chained or branched alkyl, or -O-aryl;

10 comprising the step of reacting a compound of formula I':



wherein X, Y, R², R³, and R⁴ are as defined for formula I; under conditions forming an ester or amide bond to
15 provide a compound of formula I.

37. A process for preparing a compound of formula I:



20

wherein:

X is -OR¹ or -N(R⁵)₂,

Y is halo, trifluorophenoxy, or tetrafluorophenoxy;

R¹ is:

C₁₋₆ straight chained or branched alkyl, alkenyl, or alkynyl, wherein the alkyl, alkenyl, or alkynyl is optionally substituted with optionally substituted phenyl, CF₃, Cl, F, OMe, OEt, OCF₃, CN, or

5 NMe₂;

C₁₋₆ cycloalkyl, wherein 1-2 carbon atoms in the cycloalkyl is optionally replaced with -O- or -NR⁵-;

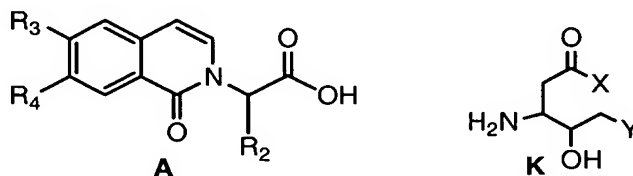
R² is C₁₋₆ straight chained or branched alkyl;

R³ is hydrogen, halo, OCF₃, CN, or CF₃;

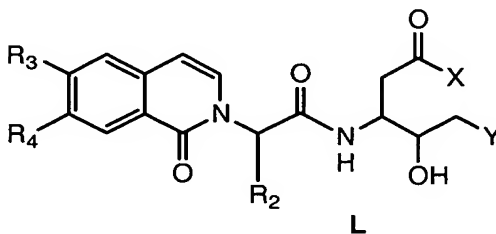
10 R⁴ is hydrogen, halo, OCF₃, CN, or CF₃; and

R⁵ is H, C₁₋₆ straight chained or branched alkyl, aryl, -O-C₁₋₆ straight chained or branched alkyl, or -O-aryl;

comprising the step of coupling a compound of
15 formula A and a compound of formula K:



to provide a compound of formula L:

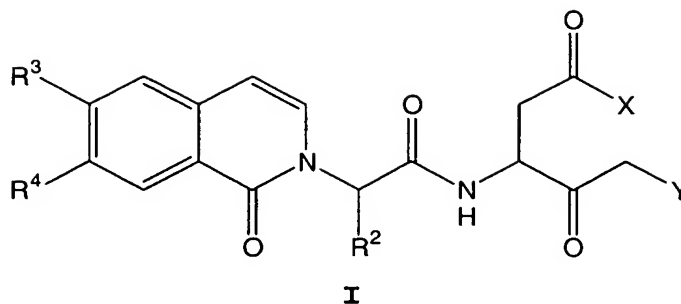


20

wherein X, Y, R¹, R², R³, and R⁴ are as defined in formula I and wherein the hydroxy group in K is optionally protected.

25

38. A process for preparing a compound of formula I:



wherein:

X is $-OR^1$ or $-N(R^5)_2$,

5 Y is halo, trifluorophenoxy, or tetrafluorophenoxy;

R^1 is:

C_{1-6} straight chained or branched alkyl, alkenyl, or alkynyl, wherein the alkyl, alkenyl, or alkynyl is optionally substituted with optionally substituted phenyl, CF_3 , Cl, F, OMe, OEt, OCF_3 , CN, or NMe_2 ;

C_{1-6} cycloalkyl, wherein 1-2 carbon atoms in the cycloalkyl is optionally replaced with $-O-$ or $-NR^5-$;

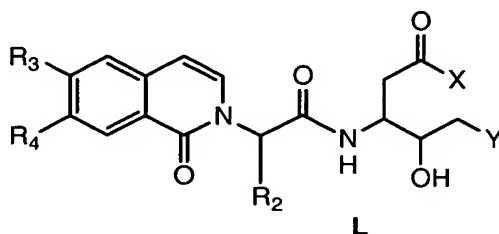
R^2 is C_{1-6} straight chained or branched alkyl;

15 R^3 is hydrogen, halo, OCF_3 , CN, or CF_3 ;

R^4 is hydrogen, halo, OCF_3 , CN, or CF_3 ; and

R^5 is H, C_{1-6} straight chained or branched alkyl, aryl, $-O-C_{1-6}$ straight chained or branched alkyl, or $-O-$ aryl;

20 comprising the step of oxidizing a compound of formula L:



wherein X, Y, R^1 , R^2 , R^3 , and R^4 are as defined for formula I; to provide a compound of formula I.